REMARKS

Claims 4 to 8 and 24 to 29 remain in the case.

Reconsideration of this Application and entry of the foregoing amendments are requested. SEQ ID Nos have been added in the description of the drawings and SEQ ID Nos in the remainder of the disclosure have been amended in accordance with the enclosed Sequence Listing. Claims 4, 8, 24, 25 and 29 have been amended in view of the Office Action and to better define what the Applicants consider their invention, as fully supported by an enabling disclosure. In particular, in the claims, the sequence numbers have been modified in accordance with the new Sequence Listing provided herewith. Support for these amendments may be found in the original claims.

The Applicants first note that the rejections under 35 USC § 112, second paragraph, and under 35 USC § 102 (b) and (a) were withdrawn and wish to thank the Examiner. The Applicants also note the Examiner's conclusion that the nucleic acid sequences of SEQ ID NO: 1 (now SEQ ID NO: 5), 3, 5 (now SEQ ID NO: 1), 7 (now SEQ ID NO: 6), and 9 (now SEQ ID NO: 7) are free of the prior art of record.

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The Examiner first notes that not all sequences were identified in the Sequence Listing and identified with SEQ ID NO. The Applicants became aware from the extract of the Sequence Listing enclosed in the Official Action, that the Examiner based its opinion on the Sequence Listing filed on March 27, 2000. However, an amended Sequence Listing was filed subsequently, namely on March 7, 2001. Please find enclosed a photocopy of the postcard establishing same. Briefly, the March 27, 2000 and the March 7, 2001 differed as follows: 1) the DNA oligonucleotides sequences appearing in the March 2001 SEQ ID NOs: 12 to 26, were correctly labelled as such in Patentin. In the March 2000 Sequence Listing, these sequences were mistakenly labelled as proteins so that the one letter nucleotides were interpreted as amino acids; 2) the March 2000 SEQ ID NO: 15 was

removed from the March 2001 Sequence Listing because it was identical to the March 2000 SEQ ID NO: 14; and 3) finally the *C. elegans* Staufen sequence was added in the March 2001 Sequence Listing.

Nevertheless, in order to comply with the Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures, a new Sequence Listing is provided herewith along with the statement under 37 CFR 1.825(a) and (b). All sequences appearing in the figures and in the disclosure are now so identified and included in the new Sequence Listing pursuant to 37 CFR 1.821. In this Sequence Listing, the original sequences were reordered, additional sequences and missing information were added, a CDS that did not correspond to any protein sequence disclosed in the specification was removed (original SEQ ID NO: 10), and duplicates for one of the protein sequences were removed (original SEQ ID NO: 8 and 2). In addition, corrections were brought to some of the sequences: 1) the starting codon in original SEQ ID NO: 1 (now SEQ ID NO: 5) and in the consequent encoded protein (original SEQ ID NO: 2, now SEQ ID NO: 4) were corrected. Support for this modification is found in the nucleotide sequence for T1 of Figure 1B, where the starting codon is correctly identified; 2) In March 2001 SEQ ID NO: 27, the stated organism was erroneous and is now correctly identified as *c. elegans* in the enclosed Sequence Listing; and 3) in the human *staufen* nucleotide sequence, the positions of nucleotides 233 and 234 were inverted in SEQ ID NOs: 1, 3 and 5 of the March 2001 Sequence Listing and are corrected in the enclosed Sequence Listing.

For the Examiner's easy reference, a table of correspondence between the SEQ ID NO: of the March 2000, the March 2001 and the enclosed Sequence Listings is provided below. As is indicated above, errors were corrected from one Sequence Listing to the next so that the correspondence between the sequences is not perfect:

TABLE OF CORRESPONDENCE

March 2000 Sequence Listing	March 2001 Sequence Listing	Enclosed Sequence Listing
1	1	5 (Human *staufen* transcript T1

		of figure 1B)
2	2	4 (Human Staufen protein encoded by transcripts T1, T2 and T4 of figure 1B)
3	3	3 (Human *staufen* transcript T2 of figure 1B)
4	4	4 (See above)
5	5	1 (Human *staufen* transcript T3 of figure 1B)
6	6	2 (Human Staufen protein encoded by transcript T3 of figure 1B)
7	7	6 (Human *staufen* transcript T4 of figure 1B)
8	8	4 (See above)
9	9	7 (*mus musculus staufen*)
10	10	Removed
11	11	8 (*mus musculus* Staufen protein)
12	12	13 (DNA oligonucleotide)
13	13	14 (*Id.*)
14	14	15 (*Id.*)
15	Removed	Removed
16	15	16 (*Id.*)
17	16	17 (*Id.*)
18	17	18 (*Id.*)
19	18	19 (*Id.*)
20	19	20 (*Id.*)
21	20	21 (*Id.*)
22	21	22 (*Id.*)
23	22	23 (*Id.*)
24	23	24 (*Id.*)
25	24	25 (*Id.*)
26	25	26 (*Id.*)
27	26	27 (*Id.*)
No equivalent	27	10 (*C. elegans* Staufen protein)
No equivalent	No equivalent	9 (*Drosophila* Staufen protein)

No equivalent	No equivalent	11 (Rat tubulin-binding domain amino acid sequence MAP1b)*
No equivalent	No equivalent	12 (Human microtubule-binding domain amino acid sequence)*

* Support can be found in Figures 1' a and b

REJECTION UNDER 35 U.S.C. § 112 FIRST PARAGRAPH

The Examiner maintains his objection to claims 4 to 8 and 24-25 based on 35 USC § 112, first paragraph. He maintains that these claims do not reasonably provide enablement for a nucleic acid encoding a Staufen polypeptide comprising amino acids 82-577 or 83-577 of SEQ ID NO: 2 (previously SEQ ID NO: 6) or other recited embodiments. He also states that it is unclear whether the fragment 83-577 would bind to dsRNA or would have any activity attributed to full length SEQ ID NO: 2. Again, although it is not specified, the Applicants understand this objection to relate to the wording of claims 4(b) and (d). The objection was maintained notwithstanding the Applicants arguments because the nexus between SEQ ID NO: 2 and figure 1b had not been disclosed. It is believed that the amended specification and Sequence Listing identifying each of the sequences displayed in figure 1b in the Sequence listing clarify the issue.

Also note that claims 4(b) and (d) have been amended as follows. The fragments 82 to 577 and 83 to 577 of SEQ ID NO: 2, are identical to the full length sequence of SEQ ID NO: 4 and fragment 2 to 496 of SEQ ID NO: 4, respectively. Because this last formulation appears clearer, claims 4(b) and (d) now recite exactly that. As the Examiner requested therefore, the amino acid numbers of the positions of RBD1 to RBD4 in SEQ ID NO: 2, 4 and fig. 1b are as follows: 1) RB1 is at 140-160 of SEQ ID NO:2; and at 59-79 in SEQ ID NO: 4 and in fig. 1b; 2) RB2 is at 183-249 of SEQ ID NO:2; and at 102-168 of SEQ ID NO: 4 and in fig. 1b; 3) RB3 is at 286-352 of SEQ ID NO: 2; and at 205-271 of SEQ ID NO: 4 and in fig. 1b; and 4) RB4 is at 533-553 of SEQ ID NO:2; and at 452-472 of SEQ ID NO: 4 and in fig. 1b. As indicated in the Table of correspondence, SEQ ID NO: 2 and 4 correspond to the human Staufen protein encoded by transcript T3, and by transcripts T1, T2 and T4 of figure 1b, respectively.

It should thus become apparent to the Examiner that the sequences of amino acids recited in claims 4(b) and (d) as well as in (a) and (c), therefore contains all four RBDs appearing in fig. 1b.

For additional clarity, the sequences of amino acids recited in claim 4(e) and (f), namely from 1 to 487 and 2 to 487 of SEQ ID NO: 8 (previously SEQ ID NO: 11), respectively, correspond to the sequences of amino acids from 1 to 487, and 2 to 487 of fig. 1c, respectively. In the same manner, the amino acids sequence recited in claim 4(g), namely the amino acids sequence of SEQ ID NO: 10 (previously SEQ ID NO:27), corresponds to the amino acid sequence of *C. elegans* appearing in fig. 1' in the alignment for CEL.

The Examiner also maintained his objection to claim 25(d). The Applicant respectfully disagrees but for the purpose of accelerating the prosecution, claim 25(d) was cancelled without prejudice and disclaimer. Applicant reserves the right to prosecute the embodiment of claim 25(d) in further applications.

REJECTION BASED ON THE USE OF THE WORDING "95% IDENTICAL"

The Examiner reiterates its rejection to claims 4 and 24 relative to the reciting of nucleotides 95% identical to recited polypeptide. The Examiner maintains his opinion that since the disclosure does not teach which 5% of the recited nucleotides could be substituted without altering the activity of the encoded protein, it is not enabling for such wording. The Applicants respectfully disagree as follows.

The Applicants reiterates that the alignment between the mouse and the human Staufen sequences at figure 1D does precisely that: it teaches which amino acids may be modified without altering the function of the protein. It is submitted that a person of ordinary skill in the art would understand from this alignment that it is likely that the amino acids that differ between the two sequences could be substituted while maintaining the biological activity of the protein. In particular, single dots between amino acids in the alignment indicates that conservative substitutions at

those positions will likely not affect the function of the protein while an absence of dots between amino acids in the alignment indicates that any substitution at those positions will likely not affect the function of the protein. It is therefore submitted that the specification shows how to make and use a Staufen protein having a 95 % identity with the disclosed sequences.

In view of the foregoing, it is believed that the rejection of the present claims under USC §112 first paragraph should be withdrawn.

NEW PARAGRAPH IN CLAIM 4 RECITING SEQUENCES HYBRIDIZING TO KNOW SEQUENCES

Claim 4 now recites in a new paragraph nucleotide sequences which hybridize under highly stringent conditions to nucleotides encoding the amino acid sequences recited in paragraphs a) to h). As indicated earlier, the Applicants note that the previous arguments presented in the June 18, 2002 response relative to the patentability of such wording in claim 24g were found persuasive by the Examiner. The Applicants wish to further add that this way of claiming nucleotide sequences was deemed acceptable by the Federal Court of Appeal in its July 2002 decision *Enzo Biochem Inc.* v. *Gen-Probe Inc.*, 63 USPQ2d 1609 (CAFC 2002). See in particular pages 1613 and 1616 wherein the Court indicates that defining nucleotide sequences by their ability to hybridize to known sequences is an acceptable way of claiming nucleotide sequences. It is further submitted that such definition meets the enablement requirement which ask that the specification show how to "make and use" the claimed sequences. A person of ordinary skill in the art can use the described sequences as probes to identify other sequences to which they would hybridize.

NEW MATTER REJECTION

The Examiner remains of the opinion that claim 4 contains subject matter which was not described in the specification. The Applicants believes that the confusion probably derived from the fact that the Sequence Listing examined by the Examiner was that filed in March 2000. In the Sequence Listing filed in March 2001, SEQ ID NO: 27 was a 705 amino acid sequence. This sequence has now been renumbered as indicated in the Table above as SEQ ID NO: 10. The Sequence Listing was

further corrected to indicate that it is a Staufen protein *C. elegans* sequence, namely that presented in Figure 1' as stated in the amended specification.

Accordingly, the Applicants therefore respectfully request that the new matter rejection of claim 4 under 35 USC §112 first paragraph be withdrawn.

CONCLUSION

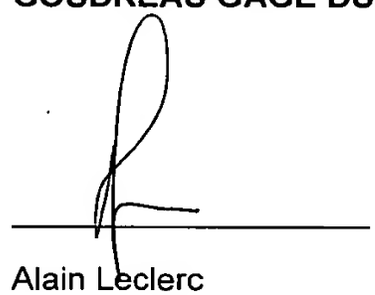
The rejections of the original claims are believed to have been overcome by the present remarks and the introduction of new claims. From the foregoing, further and favorable action in the form of a Notice of Allowance is believed to be next in order, and such an action is earnestly solicited.

It should be understood that claim amendments for which no explanation is established above were made for clarity purposes only and not for reasons related to statutory requirements for patentability.

Authorization is hereby given to charge deposit account no. 07-1742 for any deficiencies or overages in connection with this response.

Respectfully submitted,

GOUDREAU GAGE DUBUC



Alain Leclerc

Reg. No. 37,036

Date: March 7, 2003

(514) 397-7675

Encls.: Copy of post card establishing filing of March 2001 Sequence Listing

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE DISCLOSURE:

Kindly replace page 12, line 5 to page 13, line 2 by the following:

"Figure 1A shows an alignment of the two cDNAs of the human *staufen* cDNAs, designated T1 (SEQ ID NO: 1) and T2 (SEQ ID NO: 3) and ~~an amino acid sequences of the human staufen cDNAs. Alignment of the two cDNAs with~~ the translation of the putative protein sequences thereof, starting at amino acid no. –81 and 1, respectively, and presented as the amino acid sequences in SEQ ID NO: 2 and SEQ ID NO: 4, respectively. The numbers refer to the sequence of the short cDNA. The positions of the 4 dsRNA-binding consensus domains (RBD1 to RBD4) and of the tubulin-binding domain (TBD) are indicated between brackets above the sequence. The sequences were deposited in the GenBank database under accession numbers AF061938 and AF061939.

Figure 1B is similar to Figure 1 but shows the alternative splicing which occurs in the human *staufen* gene and gives rise to 4 alternatively spliced transcripts, namely T1, a 3142 bp nucleotide sequence appearing in SEQ ID NO: 5 and encoding from nucleotide 288 to 1775 the protein appearing in SEQ ID NO: 4; T2, a 3217 bp nucleotide sequence discussed above and appearing in SEQ ID NO: 3 and also encoding from nucleotide 363 to 1850 the protein appearing in SEQ ID NO: 4; T3 (designated T1 in Fig 1A), a 3506 bp nucleotide sequence appearing in SEQ ID NO: 1 and encoding from nucleotide 409 to 2139 the protein appearing in SEQ ID NO: 2; and T4, a 3348 bp nucleotide sequence appearing in SEQ ID NO: 6 and encoding from nucleotide 494 to 1981 the protein appearing in SEQ ID NO: 4. These 4 transcripts therefore give rise to the two proteins as described in Figure 1 and in the text below. ~~Of note, transcripts T2 and T3 refer to transcripts T1 and T2 of Figure 1A, respectively~~.

Figure 1C shows the nucleic acid (SEQ ID NO: 7) and predicted amino acid sequence (SEQ ID NO: 8) of mouse *staufen*.

Figure 1D shows an alignment of the mouse (SEQ ID NO: 8) and human sStaufen (SEQ ID NO: 4), highlighting the significant conservation of the

protein during evolution. As per Figure 1, the 4 dsRNA binding domains (RBD) and tubulin-binding domains are highlighted.

Figure 1' shows an alignment between phylogenetically different sStaufen proteins of *Drosophila* (SEQ ID NO: 9), *C. elegans* (SEQ ID NO: 10) and human (SEQ ID NO: 4). This alignment permits the elaboration of a consensus sequence for *staufen*. As shown in Figure 1B, T1, T2 and T4 give rise to the short protein of 55 -kDa (SEQ ID NO: 4) while T3 gives rise to the 63 kDa protein (SEQ ID NO: 2). Figure 1'B shows an alignment between a region comprising the human Staufen tubulin-binding domain (SEQ ID NO: 11) and the human MAP1B microtubule-binding domain (SEQ ID NO: 12)."

At pages 42, line 4 to p. 43, line 7, kindly replace by the following:

"annealed complementary oligonucleotides 5'-AGCTTAATTAGCTGAC-3' (SEQ ID NO:~~12~~13) and 5'-AGCTGTCAGCTAATTA-3' (SEQ ID NO:~~13~~14). The MBP/mSTAU fusion protein, containing the full-length mStau sequence, was generated by PCR amplification with Vent DNA polymerase (New England BioLabs), using the primer pair 5'-CCTGGATCCGAAAG-TATAGCTTCTACCATTG-3' (SEQ ID NO:~~14~~15) and 5'-TACATAAGCTTCTAGAT-GGCCAGAAAAGGTTCAGCA-3' (SEQ ID NO:~~15~~16). The resulting 1562 bp fragment was digested with HindIII and BamHI, and ligated in the pMal-c vector. The C-terminal fragment (mSTAU-C) was amplified with the primer pair 5'-GGATGAATCCTATTAGTAGACTTGCAC-3' (SEQ ID NO:~~16~~17) and 5'-TACATAAGC-TTCTAGATGGCCAGAAAAGGTTCAG-CA-3' (SEQ ID NO:~~22~~23), digested with HindIII and cloned in the EagI* and HndIII sites of pMal-c. EagI* was created by filling in the cohesive ends of EagI-digested pMal-c vector using the Klenow fragment of DNA polymerase I. This fusion vector was then digested with SacI and EcoRI and the resulting fragment was subcloned in the pMal-stop vector to generate the mSTAU-RBD3 construct. The mSTAU-TBD construct was prepared by PCR using the primer pair 5'-GCTCTAGATTCAAAG-TTCCCCAGGC-GCAG-3' (SEQ ID NO:~~17~~18) and 5'-TTTAAGCTTCTCAGA-GGGTCTAGT-GCGAG-3' (SEQ ID NO:~~18~~19); the product was digested with XbaI and HindIII and cloned in the pMal-stop vector. mSTAU-RBD2 and mSTAU-RBD1 were constructed by first

amplifying a fragment using the primer pair 5'-CAATGTATAAGCCCGTGGACCC-3' (SEQ ID NO:~~19~~20) and 5'-AAAAAGCTTGTGCAAGTCTACTAATAGGATTCACC-3' (SEQ ID NO:~~20~~21). The resulting product was digested with HindIII and cloned in the EagI* and HindIII sites of the pMal-stop vector. This vector was then used to purify the 398 bp PstI and HindIII fragment, which was subcloned in the pMAL-stop vector to generate the mSTAU-RBD2 construct. In the same way, the mSTAU-RBD1 vector was obtained by digestion with SmaI and StuI, followed by recircularization of the digestion product using T4 DNA ligase. The mSTAU-RBD4 was PCR amplified using the primer pair 5'-ATAGCCCGAGAGTTGTTG-3' (SEQ ID NO:~~21~~22) and 5'-TACAT-AAGCTTCTAGATGGC-CAGAAAAGGTTCAGCA-3' (SEQ ID NO:~~22~~23)."

Kindly replace pages 45, lines 13 to 24 by the following:

"5'-TACATGTCGACTTCCTGCCA/GGGCTGCGGG-3' (SEQ ID NO:~~23~~24) and 5'-TACAATCTAGATTATCAGCGGCCGCACCTCCCACACACAGACAT-3' (SEQ ID NO:~~24~~25). The 3'-primer was synthesized with a NotI site just upstream from the stop codon allowing ligation of a NotI cassette containing either three copies of the HA-tag or the GFP sequence. The resulting fragment was cloned in Bluescript following digestion with SalI and XbaI. The KpnI/XbaI fragment was then subcloned in the pCDNA3/RSV vector (Jockers et al., 1996) and a NotI-cassette was introduced at the NotI site. For the TBD/GFP fusion protein, the TBD was PCR-amplified with oligonucleotides on each side of this region (SEQ ID NO:~~25~~—26 (5'-TACATAAGCTTAAGCCACCATGGTCAAAGTTCC-CCAGGCGC-3') and (SEQ ID NO:~~26~~—27 5'- TACAATC-TAGAGCGGCCGCGCTCAGAGGGTCTAGTGCGA-G-3')."

IN THE CLAIMS:

Claims 4, 8, 24, 25 and 29 have been amended as follows: Underlines indicate insertions and ~~strikethrough~~ indicate deletions.

4. (Thrwice amended) An isolated nucleic acid molecule comprising a polynucleotide sequence at least 95% identical to a sequence selected from the group consisting of :

(a) a nucleotide sequence encoding a ~~staufen~~ Staufen polypeptide comprising amino acids from 1 to 577 of SEQ ID NO:~~6~~2;

(b) a nucleotide sequence encoding a ~~staufen~~ Staufen polypeptide comprising the sequence of amino acids ~~from 82 to 577~~ of SEQ ID NO:~~6~~4;

(c) a nucleotide sequence encoding a ~~staufen~~ Staufen polypeptide comprising amino acids from 2 to 577 of SEQ ID NO:~~6~~2;

(d) a nucleotide sequence encoding a ~~staufen~~ Staufen polypeptide comprising amino acids from ~~83 to 577~~2 to 496 of SEQ ID NO:~~6~~4;

(e) a nucleotide sequence encoding a ~~staufen~~ Staufen polypeptide comprising the sequence of amino acids ~~from 1 to 487~~ of SEQ ID NO:~~1~~18;

(f) a nucleotide sequence encoding a ~~staufen~~ Staufen polypeptide comprising amino acids from 2 to 487 of SEQ ID NO:~~1~~18;

(g) a nucleotide sequence encoding a ~~staufen~~ Staufen polypeptide comprising the amino acid sequence of SEQ ID NO:~~2~~710;

~~(h) a nucleotide sequence encoding a staufen polypeptide comprising the amino acids from 1 to 591 of SEQ ID NO:2; and~~

~~(i)~~(h) a nucleotide sequence encoding a ~~staufen~~ Staufen polypeptide comprising a nucleotide sequence complementary to any of the nucleotide sequences in (a), (b), (c), (d), (e), (f) or (g) ~~or (h)~~; and

i) a sequence which hybridizes under high stringency conditions to the sequence in (h).

5. A recombinant vector comprising said isolated nucleic acid molecule of claim 4.

6. A method of making a recombinant host cell comprising introducing the recombinant vector of claim 5 into a host cell.

7. A recombinant host cell produced by the method of claim 6.

8. (Amended) A recombinant method for producing ~~staufen~~ Staufen polypeptide, comprising culturing said host cell of claim 7 under conditions such that said polypeptide is expressed and recovering said ~~staufen~~ Staufen polypeptide.

24. (Amended) An isolated nucleic acid molecule comprising a polynucleotide sequence which encodes a ~~s~~Staufen polypeptide, said polynucleotide sequence being ~~at least 95%~~ identical to a sequence selected from the group consisting of:

(a) SEQ ID NO:~~1~~5;

(b) SEQ ID NO:3;

(c) SEQ ID NO:~~5~~1;

(d) SEQ ID NO:~~7~~6;

(e) SEQ ID NO:~~9~~7;

(f) a nucleotide sequence complementary to any of the nucleotide sequences in (a), (b), (c), (d), or (e); and

(g) a sequence which hybridizes under high stringency conditions to the sequence in (f).

25. (Twice Amended) An isolated nucleic acid molecule comprising a polynucleotide sequence selected from the group consisting of:

(a) a nucleotide sequence encoding a ~~s~~Staufen polypeptide comprising the sequence of amino acids ~~1 to 591~~ of SEQ ID NO:~~2~~4;

(b) a nucleotide sequence encoding a S~~s~~taufen polypeptide comprising the sequence of amino acids ~~1 to 577~~ of SEQ ID NO:~~6~~2;

(c) a nucleotide sequence encoding a S~~s~~taufen polypeptide comprising amino acids 2 to 577 of SEQ ID NO:~~6~~2; and

(d) a nucleotide sequence encoding a ~~s~~Staufen polypeptide and conservative substitutions of the polypeptides encoded by any of the sequences in (a), (b) or (c).

26. A recombinant vector comprising said isolated nucleic acid molecule of claim 24.

27. A method of making a recombinant host cell comprising introducing the recombinant vector of claim 26 into a host cell.

28. A recombinant host cell produced by the method of claim 27.

29. A recombinant method for producing ~~staufen~~ Staufen polypeptide, comprising culturing said host cell of claim 28 under conditions such that said polypeptide is expressed and recovering said ~~staufen~~ Staufen polypeptide.